UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/830,514	04/27/2001	Jurgen Rabenhorst	3968.057	8206

7590 06/02/2005

PENDORF & CUTLIFF
5111 MEMORIAL HIGHWAY
TAMPA, FL 33634-7356

EXAMINER	
RAMIREZ, DELIA M	

ART UNIT	PAPER NUMBER
1652	

DATE MAILED: 06/02/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/830,514	RABENHORST ET AL.	
	Examiner	Art Unit	
	Delia M. Ramirez	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *07 March 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *17 and 19-31* is/are pending in the application.

4a) Of the above claim(s) *24-28* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *17,19-23 and 29-31* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *07 March 2005* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

RD

DETAILED ACTION

Status of the Application

Claims 17 and 19-31 are pending.

Applicant's amendment of claims 17, 19-23, 29-31, amendments to the specification, and submission of drawings in a communication filed on 3/7/2005 are acknowledged.

This application contains claims 24-28 drawn to an invention non-elected with traverse in a communication filed on 9/2/2004. A complete reply to the final rejection must include cancellation of non-elected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

Rejections and/or objections not reiterated from previous office actions are hereby withdrawn.

Drawings

1. The replacement drawings corresponding to Figures 2a-2r submitted on 3/7/2005 are accepted by the Examiner.

Claim Objections

2. Claim 21 is objected to due to the recitation of "selected from the group consisting of a microorganism....or animal cell". It is suggested that the term be amended to recite "selected from the group consisting of a microorganism....and animal cell". Appropriate correction is required.

3. Claim 29 is objected due to the recitation of "by inserting of Ω elements". It is suggested that the term be amended to recite ""by inserting Ω elements" or "by insertion of Ω elements". Appropriate correction is required.

Claim Rejections - 35 USC § 112, Second Paragraph

4. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. Claims 29-30 remain rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

6. Claim 29 remains indefinite in the recitation of "process for the biotechnological preparation of alcohols...comprising adding an organism.....such that intermediates...accumulate". As previously indicated, while the preamble indicates that the claimed process is for the preparation of any alcohol, aldehyde and organic acid, there is no step indicating how the intermediates recited are transformed into any alcohol, aldehyde or organic acid. It is noted that since the process requires an organism which is modified such that coniferyl alcohol, coniferyl aldehyde, ferulic acid, vanillin and/or vanillic acid accumulate, the only compounds which can be made by the claimed method as written are coniferyl alcohol, coniferyl aldehyde, ferulic acid, vanillin and/or vanillic acid. Also, there is no step indicating the isolation of the recited compounds. It is suggested that the claim be amended to recite "process for the biotechnological preparation of coniferyl alcohol, coniferyl aldehyde, ferulic acid, vanillin or vanillic acid ...comprising (1) cultivating an organism.....such that intermediates...accumulate, and (2) isolating the intermediates". Correction is required.

7. Claim 30 remains indefinite in the recitation of "wherein the alteration in eugenol...catabolism is achieved by microbiological methods, wherein said methods are used to further culture said organism". As previously indicated, it is unclear as to which microbiological culturing methods would allow one of skill in the art to insert Ω elements or deletions in a gene. Applicants argue that the claim has been amended to indicate that the microbiological culturing methods are used to further propagate the claimed microorganism. Applicants also argue that microbiological culturing methods are well known in the art whereby mutants with gene deletions or extra-gene elements may be further propagated. Applicants also refer to Example 6 of the specification where conjugation of mutants is described. Arguments have been

fully considered but are not deemed persuasive. The Examiner acknowledges Example 6 and agrees that culturing methods would allow propagation (i.e. cell growth) of the claimed organism. However, it is unclear to the Examiner as to which microbiological culturing methods would allow the mutations required in the claimed organism to occur. The term "microbiological culturing method" implies commonly used techniques for growing/propagating a cell. While some microbial culturing methods may result in mutagenesis of a microorganism since a mutagen can be added to the culture medium (e.g. chemical mutagenesis), the organism of claim 17 requires insertion of Ω elements or deletions. While one could envision the use of bacterial conjugation as described in Example 6 to obtain a microorganism as claimed, one of skill in the art would not considered bacterial conjugation a microbiological culturing method. It is noted that "culturing" an organism is not the same as "mutating/modifying" an organism. For examination purposes, no patentable weight will be given to the term "wherein the alteration in eugenol...catabolism is achieved by microbiological methods, wherein said methods are used to further culture said organism". Correction is required.

Claim Rejections - 35 USC § 112, First Paragraph

8. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

9. Claims 17, 19-23, 29-31 remain rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This rejection has been discussed at length in the Non Final Action mailed on 11/3/2004.

10. Applicants argue that the claims have been amended to emphasize that the organisms claimed are those in which the enzymes of the eugenol/ferulic acid catabolism have been inactivated by inserting Ω

elements or introducing deletions into the genes encoding such enzymes. Applicants also argue that they are not claiming a genus of genes encoding enzymes of the eugenol/ferulic acid catabolism pathway but rather transformed organisms in which the genes encoding enzymes of the eugenol/ferulic acid catabolism pathway have been inactivated.

11. Applicant's arguments have been fully considered but are not deemed persuasive to overcome the instant rejection. The Examiner acknowledges the amendments to the claims and agrees that the claims are not directed to a genus of genes encoding enzymes of the eugenol/ferulic acid catabolism pathway. However, it is noted that the genus of genes recited must be adequately described for the claimed invention to be adequately described since the genus of genes recited is required by the claimed invention. It is noted that inactivation by deletion or by insertion of Ω elements would require some knowledge of the structure of the target gene. The specification fails to disclose the structures of the required genes and there is no representative structure of all the genes required taught by the art or the specification. It is reiterated herein that the genus of genes required is extremely large and structurally variable. The disclosure of a single species of the claimed organism and a single species of a gene encoding coniferyl alcohol dehydrogenase (calA), coniferyl aldehyde dehydrogenase (calB), feruloyl-CoA synthase (fcs), enoyl-CoA hydratase-aldolase (ech), vanillin dehydrogenase (vdh), or beta-ketothiolase (aat) is insufficient to put one of skill in the art in possession of all attributes and features of the claimed invention.

12. Claims 17, 19-23, 29-31 remain rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for (1) a transformed Pseudomonas sp. HR199 as described in the specification, wherein said strain contains at least one inactivated gene encoding coniferyl alcohol dehydrogenase (calA), coniferyl aldehyde dehydrogenase (calB), feruloyl-CoA synthase (fcs), enoyl-CoA hydratase-aldolase (ech), vanillin dehydrogenase (vdh), or beta-ketothiolase (aat), wherein said gene

inactivation is due to the introduction of deletions or insertional mutagenesis with Ω elements, (2) a method of using said Pseudomonas strain for the production of coniferyl alcohol, coniferyl aldehyde, ferulic acid, vanillin and/or vanillic acid, and (3) a method of making the strain of (1), does not reasonably provide enablement for (a) any unicellular or multicellular organism modified such that any enzyme associated with eugenol and/or ferulic acid catabolism is inactivated by inserting Ω elements or deletions in the genes encoding said enzymes, and wherein the intermediates coniferyl alcohol, coniferyl aldehyde, ferulic acid, vanillin and/or vanillic acid accumulate, (b) any unicellular or multicellular organism modified such that any gene encoding coniferyl alcohol dehydrogenase, coniferyl aldehyde dehydrogenase, feruloyl-CoA synthase, enoyl-CoA hydratase-aldolase, vanillin dehydrogenase, or beta-ketothiolase is inactivated by insertion of Ω elements or deletions, (c) a method to produce coniferyl alcohol, coniferyl aldehyde, ferulic acid, vanillin and/or vanillic acid with the organisms of (a) or (b), or (d) a method of making the organisms of (a) or (b). The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or the invention commensurate in scope with these claims. This rejection has been discussed at length in the Non Final Action mailed on 11/3/2004.

13. Applicants argue that the novelty of the invention is mutant organisms in which Ω elements have been inserted or deletions have been introduced to inactivate the genes encoding enzymes of the eugenol/ferulic acid catabolism pathway such that the intermediate products accumulate. According to Applicants, the techniques and methods used in the present invention are well known in the art and that these methods as well as those described in the specification can be applied to other organisms, including the insertion of Ω elements.

14. Applicant's arguments have been fully considered but are not deemed persuasive to overcome the instant rejection. The Examiner acknowledges that the claimed invention requires inactivation of the genes encoding enzymes of the eugenol/ferulic acid catabolism pathway such that the intermediate

products accumulate, and agrees that the techniques used in the present invention are well known in the art, such as introduction of deletions or insertion of Ω elements for gene inactivation. However, the Examiner disagrees with the notion that the claimed invention is fully enabled by the teachings of the specification. As indicated above, inactivation by deletion or by insertion of Ω elements would require some knowledge of the structure of the target gene. In fact, the specification teaches that to create the modified Pseudomonas cell of the invention, the required genes were first isolated prior to inactivation. However, the specification fails to disclose the structures of all the recited genes and there is no representative structure of all the genes required taught by the art or the specification. It is reiterated herein that the genus of genes required is extremely large and structurally variable but the specification fails to provide some guidance or teaching as to a correlation between structure and function for all the genes encompassed by the claims. The disclosure of a single species of the claimed organism and a single species of a gene encoding coniferyl alcohol dehydrogenase (calA), coniferyl aldehyde dehydrogenase (calB), feruloyl-CoA synthase (fcs), enoyl-CoA hydratase-aldolase (ech), vanillin dehydrogenase (vdh), or beta-ketothiolase (aat) is not sufficient to provide one of skill in the art with guidance to enable the full scope of the claimed invention. Thus, one of skill in the art would have to go through the burden of undue experimentation to practice the full scope of the claimed invention.

15. It is reiterated herein that if the claims were to be amended to refer specifically to Pseudomonas sp. HR199, a biological deposit may be required to satisfy the enablement requirements set forth in 35 USC 112, first paragraph.

Claim Rejections - 35 USC § 102

16. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

17. Claim 29 was rejected under 35 U.S.C. 102(b) as being anticipated by Priefert et al. (J. Bacteriol. 179(8):2592-2607, 1997; previously cited by the Examiner). This rejection has been discussed at length in the Non Final Action mailed on 11/3/2004.

18. Applicants argue that the claim has been amended to recite the method used for inactivating the enzymes of the eugenol/ferulic acid catabolism pathway, which is not taught by Priefert et al.

19. Claim 29 as amended now requires inactivating the enzymes of the eugenol/ferulic acid catabolism pathway by inserting Ω elements or introducing deletions in the genes encoding said enzymes. Since Priefert et al. does not teach this limitation, this rejection is hereby withdrawn. The amended claim however will be rejected under 35 USC 103(a) for the reasons set forth below.

Claim Rejections - 35 USC § 103

20. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

21. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

22. Claim 29 as amended is rejected and claims 17, 19-23, 30-31 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Priefert et al. (J. Bacteriol. 179(8):2592-2607, 1997; previously cited

by the Examiner) in view of Blondelet-Rouault et al. (Gene 190:315-317, 1997). This rejection as it relates to claims 17, 19-23, 30-31 has been discussed at length in the Non Final Action mailed on 11/3/2004. It is now applied to amended claim 29 for the reasons set forth below.

23. As previously indicated, Priefert et al. teaches the chemical mutagenesis of Pseudomonas sp. HR 199 wherein the vdh gene is inactivated (page 2595; Abstract; Materials and Methods). The vdh gene encodes vanillin dehydrogenase which catalyzes the formation of vanillic acid (Figure 1, page 2596). Inactivation of this enzyme would allow for the accumulation of vanillin since vanillic acid cannot be formed. Priefert et al. does not teach inactivation of the vdh gene by insertion of Ω elements or by introducing deletions. Blondelet-Rouault et al. teaches antibiotic resistance gene cassettes which contain Ω elements to allow for insertional mutagenesis (Abstract, page 315). Blondelet-Rouault et al. does not teach a Pseudomonas strain which has been mutagenized to inactivate the vdh gene.

Claim 29 is directed in part to a process for the production of coniferyl alcohol, coniferyl aldehyde, ferulic acid, vanillin and/or vanillic acid wherein an organism is modified such that enzymes involved in the catabolism of eugenol and/or ferulic acid are inactivated by inserting Ω elements or introducing deletions in the genes encoding said enzymes.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to use the antibiotic resistance gene cassettes of Blondelet-Rouault et al. for insertional mutagenesis of the vdh gene in the Pseudomonas strain of Priefert et al. to produce vanillin. A person of ordinary skill in the art is motivated to use the antibiotic resistance gene cassettes of Blondelet-Rouault et al. for insertional mutagenesis of the vdh gene in the Pseudomonas strain of Priefert et al. for the benefit of being able to select those mutants which have the inactivated vdh gene using antibiotic-containing medium. One of ordinary skill in the art has a reasonable expectation of success at using insertional mutagenesis to disrupt the vdh gene in Pseudomonas with the antibiotic resistance gene cassettes of Blondelet-Rouault et al. since Ω elements (Ω interposon) for insertion mutagenesis in bacteria is well known and widely used in

the art (page 315, right column, first paragraph). Therefore, the invention as a whole would have been prima facie obvious to a person of ordinary skill in the art at the time the invention was made.

24. In regard to claims 17, 19-23, 30-31, Applicants argue that neither of the two references suggests or motivates combining them and that Priefert et al. does not teach the specific inactivation of the genes encoding coniferyl alcohol dehydrogenase, coniferyl aldehyde dehydrogenase, feruloyl-CoA synthase, enoyl-CoA hydratase-aldolase, vanillin dehydrogenase, vanillic acid demethylase or beta-ketothiolase by insertion of Ω elements and/or deletions in said genes.

25. Applicant's arguments have been fully considered but are not deemed persuasive to avoid the rejection of claim 29 or avoid the rejection of claims 17, 19-23, 30-31. The Examiner acknowledges that Priefert et al. does not teach every limitation of the claimed invention. However, the teachings of Priefert et al. in combination with those of Blondelet-Rouault et al., as previously indicated, render the claimed invention obvious because inactivation of genes by using Ω elements and by inserting deletions is well known and widely used in the art. In fact, Applicants in their response regarding the enablement rejection agree that these methods of gene inactivation are well known in the art (see page 23, third paragraph of the response). It is reiterated herein that a person of ordinary skill in the art is motivated to use the antibiotic resistance gene cassettes of Blondelet-Rouault et al. for insertional mutagenesis of the vdh gene in the Pseudomonas strain of Priefert et al. for the benefit of being able to select those mutants which have the inactivated vdh gene using antibiotic-containing medium. There is a reasonable expectation of success in inactivating the vdh gene in the Pseudomonas strain of Priefert et al. Therefore, the invention as a whole would have been prima facie obvious to a person of ordinary skill in the art at the time the invention was made.

Conclusion

26. No claim is in condition for allowance.

27. Applicant's amendment of claims 17, 19-23, 29-31 necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

28. Certain papers related to this application may be submitted to Art Unit 1652 by facsimile transmission. The FAX number is (571) 273-8300. The faxing of such papers must conform with the notices published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 CFR 1.6(d)). NOTE: If Applicant submits a paper by FAX, the original copy should be retained by Applicant or Applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED, so as to avoid the processing of duplicate papers in the Office.

29. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PMR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

30. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Delia M. Ramirez whose telephone number is (571) 272-0938. The examiner can normally be reached on Monday-Friday from 8:30 AM to 5:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. Ponnathapura Achutamurthy can be reached on (571) 272-0928. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (571) 272-1600.

Delia M. Ramirez, Ph.D.
Patent Examiner
Art Unit 1652

DR
May 25, 2005

REBECCA E. PROUTY
PRIMARY EXAMINER
GROUP 1600
1600